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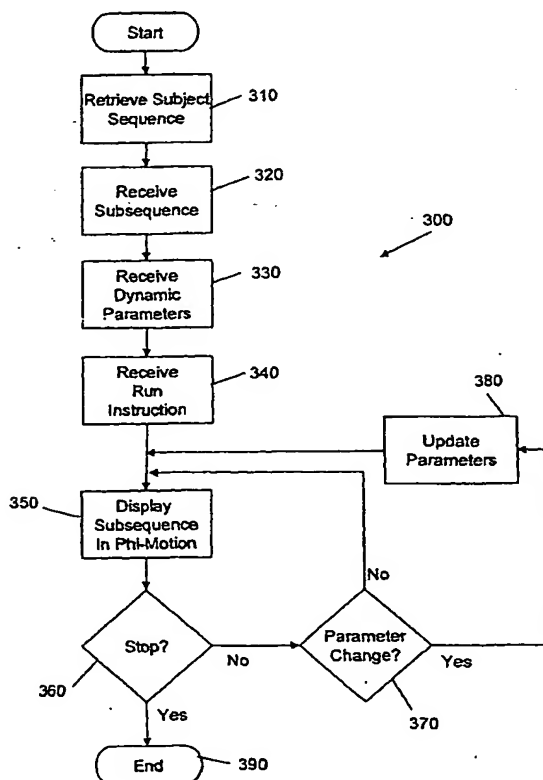
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(54) Title: **SYSTEM AND METHOD FOR VISUALIZING FLUID FLOW THROUGH VESSELS**



(57) Abstract: A method for visualizing fluid flow through vessels having a visualizing composition flowing therethrough, the method comprising the steps of: selecting from a sequence of angiographic images a subsequence of angiographic images, reading a plurality of dynamic parameters, the dynamic parameters for controlling display of the angiographic images, serially displaying the subsequence repetitively in accordance with the dynamic parameters, and providing an interface for dynamic user update of the dynamic parameters while displaying the subsequence.

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**SYSTEM AND METHOD FOR VISUALIZING  
FLUID FLOW THROUGH VESSELS**

0001 This application claims priority from United States Patent Application No. 60/365,547 filed on March 20, 2002.

- 5 0002 This invention relates to a computer aided system and method for visualizing flow in fluid carrying vessels in animal tissue and more particularly to a system and method for visualizing and identifying a direction of blood-flow in vessels supplying blood to a lesion, such as a neovascular lesion associated with age-related macular degeneration, to assist diagnosis and treatment of such lesions.

10

**BACKGROUND OF THE INVENTION**

- 0003 Lesions are normally defined as an abnormal tissue structure located in an organ or other body part, and are often a manifestation of a harmful condition, disease or illness. Lesions may take many specific forms, such as choroidal neovascularizations  
15 ("CNVs") which are found in the eye. In general, any abnormal vasculature in a body is a type of lesion.

- 0004 A CNV is one manifestation of age related macular degeneration ("AMD") and is a common cause of vision loss in people over the age of 50. In 1995, of the estimated 34 million people in the United States who were age 65 or older, approximately 1.7 million  
20 had some visual impairment resulting from AMD. Timely diagnosis and treatment of CNV is an important therapeutic objective because permanent vision loss can result if hemorrhage of the CNV occurs.

*Visualization of the CNV*

- 0005 Visualization is a process of obtaining and viewing an angiographic image  
25 representation of the blood vessels in a region of interest following introduction of a visual enhancement material into such vessels.

- 0006 Ordinarily, the choroidal vasculature of the eye cannot be readily visualized because the pigments in the retinal pigment epithelium ("RPE") layer (sandwiched between the sensory retina and the choriocapillaris) and the pigments in the choroid do  
30 not readily transmit visible light wavelengths. Therefore, even sodium fluorescein

angiography, routinely used to demonstrate the retinal vascular blood flow and whose excitation and emission spectra are comprised of visible wavelengths, shows only a faint diffuse flush resulting from vascular staining with fluorescein dye as it transits through the choroidal circulation and before dye enters the more superficial retinal vasculature.

5 0007 Another methodology, termed indocyanine green ("ICG") dye angiography ("ICGA"), is used for routinely visualizing choroidal blood flow. It is based on use of the near-infrared fluorescent light wavelengths emitted by ICG, which readily penetrate the pigmented ocular tissues. The impetus for developing ICGA about 30 years ago was to provide a tool for studying choroidal hemodynamics and blood flow physiology, but  
10 during the past 5 years, as a result of the equipment to implement it having become commercially available, its clinical use has become wide spread for detecting and monitoring AMD-associated CNV.

0008 Visualizing and monitoring CNV blood flow has become an important part of diagnosing and treating CNV, especially when the lesions are directly beneath or  
15 immediately adjacent to the foveal area of the retina.

0009 The commercial availability of the scanning laser ophthalmoscope (SLO) contributed to an increasing interest in ICGA. Compared to the predominantly available commercial ICGA systems based on fundus camera optics—capable of acquiring images at a rate of about one per second—the SLO afforded the ability to perform high-speed  
20 imaging. Ready access to high-speed ICG image acquisition systems was an important component of interest in a new AMD treatment modality, namely CNV feeder vessel photocoagulation treatment.

#### *CNV Feeder Vessel Photocoagulation*

0010 A recent approach being pursued is so-called feeder vessel ("FV")  
25 photocoagulation, wherein the afferent vessel supplying blood to the sub-foveal CNV is photocoagulated at a site outside the foveal area. So far, FV photocoagulation has proven to be an apparently effective treatment for CNVs, often resulting in improved visual acuity - a result not usually associated with other forms of treatment that have been used or considered to date. This treatment method is of particular interest for occult  
30 subfoveal CNV, for which there is no other treatment approach at this time.

0011 As mentioned earlier, FVs are those vessels identified as supplying blood to an area of CNV. The length of these vessels are on the order of one-half to several millimeters long, and are thought to lie in Sattler's layer of the choroid (See: Flower R.W., *Experimental Studies of Indocyanine Green Dye-Enhanced Photocoagulation of Choroidal Neovascularization Feeder Vessels*, Am. J. Ophthalmol., 2000, 129:501-512; which is incorporated herein by reference). Note that Sattler's layer is the middle layer of choroidal vessels containing the arterial and venous vessels that feed and drain blood from the thin layer of choroidal capillary vessels lying just beneath the sensory retina. Following visualization of a CNV feeder vessel, e.g. by ICGA, photocoagulation of the feeder vessel is then performed in order to reduce or stop the flow of blood to the CNV.

0012 Studies indicate often-dramatic resolution of the CNV-associated retinal edema and stabilization or even improvement in visual acuity, often within hours of feeder vessel photocoagulation.

0013 A major drawback to FV treatment as currently practiced is that it is necessarily limited by the accurate identification and visualization of the FVs that supply blood to a given lesion. Thus, the success of both FV photocoagulation, and alternatives such as FV dye-enhanced photocoagulation ("DEP"), hinges on proper identification of the FVs. Conventionally, a single angiogram following single large ICG bolus injection are used to locate and identify feeder vessels. This single angiogram (one sequence of angiographic images) using conventional methods is insufficient to obtain proper blood flow data, thus necessitating the use of multiple angiographic sequences on the same eye. Furthermore, choroidal tissue staining produced by a single large dye bolus using conventional methods produces images of such poor contrast that accurate FV identification is difficult. Thus, after performing one angiogram, it is often necessary to perform a second angiogram in order to obtain a second set of angiographic images. This is often necessary because the first set of images is of insufficient quality to identify a FV. Thus, the parameters are adjusted for the second angiogram, based on the outcome of the first set of images, in order to acquire better quality images and thus adequate data about lesion blood flow. Accordingly, if the second set of angiographic images from the second angiogram is still inadequate for FV identification, a third angiogram must be performed. In addition, repeated angiogram studies result in declining contrast and image quality.

0014 Even after obtaining technically adequate angiographic image sequences, sure identification of CNV FVs (as opposed to the draining vessels) is often difficult, especially when dye transits the FVs in pulsatile fashion and in the presence of significant background dye fluorescence from underlying choroidal vasculature. Under  
5 such circumstances, it is usually not possible to identify either specific feeder vessels or the direction of flow through them.

0015 Current techniques for identifying and visualizing FVs are limited. A need therefore exists for, and it is an object of the present invention to offer, improved identification of feeder vessels and visualization of the direction of blood flow through  
10 vessels.

### SUMMARY OF THE INVENTION

0016 It is an objective of this invention to provide a system and method for visualizing fluid carrying vessels in animal tissue and more particularly to provide a system and  
15 method for visualizing and identifying a direction of blood-flow in vessels supplying blood to a lesion

0017 Another objective of this invention is to significantly increase the frequency with which potentially treatable feeder vessels of a lesion can be detected. It is a further object of the invention to significantly increase the frequency with which potentially treatable  
20 feeder vessels of juxta- and sub-foveal age-related macular degeneration associated CNV can be detected.

0018 The method of the invention is based on the premise that one can more readily identify FVs, and the visualization of dye through blood vessels is generally augmented by, serially displaying a series of angiographic images, of the dye flowing through the  
25 area of interest, repetitively, while being able to manipulate certain parameters in real-time. The serial display of images is generally referred to as phi-motion.

0019 In accordance with one broad aspect of the present invention, there is provided a method for visualizing fluid flow through vessels having a visualizing composition flowing therethrough. The method comprises the following steps. Selecting from a  
30 sequence of angiographic images a subsequence of angiographic images. Reading a plurality of dynamic parameters, said dynamic parameters for controlling display of said

angiographic images. Serially displaying said subsequence repetitively in accordance with said dynamic parameters. And providing an interface for dynamic user update of said dynamic parameters while displaying said subsequence. This method is referred to as Interactive Phi-Motion ("IPM").

- 5    0020 In one embodiment of the invention, dynamic parameters consisting of speed, interval, direction and pixel brightness are used and are dynamically adjustable. Preferably, the pixel brightness relationship, between collected and displayed intensity values, is represented by and manipulable through a Look-Up Table ("LUT").

- 10   0021 Also provided is an apparatus for carrying out the inventive method, a computer program product comprising a memory with code embodied thereon corresponding to the method, and a computer readable memory storing instructions corresponding to the method.

- 15   0022 According to another broad aspect of the invention, a method is provided for treating a lesion with at least one blood vessel feeding blood to it. This method comprises: administering a visualizing composition comprising a fluorescent dye; capturing a plurality of angiographic images of a pre-selected area surrounding the lesion; visualizing the flow of said visualizing composition through said lesion using IPM; identifying said blood vessel; applying energy to said blood vessel, of a type and an amount sufficient to reduce the rate of blood flow through said blood vessel.

- 20   0023 Advantageously, the methods of the present invention offer many benefits over conventional methods. First, by displaying the angiographic images in phi-motion and manipulating the dynamic parameters in real-time, visualization of the vessels of interest and the dye front entering and filling up the vessels can be optimized. Second, only one set of high-speed angiographic images need be taken, thus obviating the need to adjust  
25   parameters between captures in order to optimize visualization based on the previous angiogram. Third, by the ability to visualize the dye wavefront, the direction of flow in the vessel can be determined with certainty, thereby assuring that afferent and not efferent vessels are treated.

- 30   0024 Still further advantages and benefits of the present invention will become apparent to those of ordinary skill in the art upon reading and understanding the following detailed description of the preferred embodiments.

**BRIEF DESCRIPTION OF THE DRAWINGS**

0025 These and other features of the preferred embodiments of the invention will become more apparent in the following detailed description in which reference is made  
5 to the appended drawings wherein:

0026 Figure 1 illustrates, in flow chart form, a method of treatment of a blood vessel supplied lesion by photocoagulation incorporating the use of IPM.

0027 Figure 2 illustrates, in flow chart form, the method of IPM.

0028 Figure 3 illustrates the default LUT according to one embodiment of IPM.

10 0029 Figure 4 illustrates a modified LUT according to one embodiment of IPM.

0030 Figure 5 illustrates a second modified LUT according to one embodiment of IPM.

0031 Figure 6 illustrates a system overview diagram of a preferred embodiment of the diagnoses and treatment of a patient with an AMD-related CNV using IPM.

0032 Figure 7 illustrates a graphical user interface of a preferred embodiment of IPM.  
15

**DESCRIPTION OF THE PREFERRED EMBODIMENTS**

0033 In the following description, numerous specific details are set forth to provide a thorough understanding of the invention. However, it is understood that the invention may be practiced without these specific details. In other instances, well-known processes  
20 have not been described or shown in detail in order not to obscure the invention. In the description and drawings, like numerals refer to like structures or and/or processes.

0034 The methods of the present invention are claimed and described herein as a series of steps. It should be understood that these methods and associated steps may be performed in any logical order that preserves the spirit of the invention. Moreover, the  
25 methods may be performed alone, or in conjunction with other procedures and treatments administered before, during or after such methods and steps set forth herein without departing from the scope and spirit of the invention. Further, it is contemplated that the term animals as used herein includes, but is not limited to, humans.



0035 Lesions, such as AMD-related CNV, have been shown to be successfully treated by photocoagulation or DEP of the blood vessel that feeds the lesion. Successful treatment, however, is predicated on the accurate and precise identification of the FV that supplies blood to the lesion. To this end, it is advantageous to both identify vessels that  
5 lead to the lesion and the direction of blood through that vessel, in order to determine whether it is a feeding (afferent) or draining (efferent) vessel. The possibility of achieving even more effective treatment of lesions, such as AMD-related CNV, lies in the improved visualization and identification of FVs using Interactive Phi-Motion prior to treatment. IPM provides improved visualization of dye flow through blood vessels, in  
10 a region of interest, by playing a subsequence of previously captured high-speed angiographic images repetitively, such as in a continuous loop, while providing the ability to dynamically manipulate certain parameters. By dynamically changing these parameters, one can find the precise combination of such parameters that will optimize the visualization of FVs for each given case. This is important as the degree to which  
15 these parameters need to be adjusted will vary with each set of angiograms, since visualization will vary depending on many variables, such as the specific patient, dose of the visualizing dye, speed at which the images were captured...etc.

0036 Referring to figure 1, one broad aspect of the present invention provides a method for treating a lesion in an animal 100. For the method to be effective, the lesion  
20 should further have a blood vessel that carries blood into the lesion. The inventive method includes, but is not limited to, the following steps. Performing high-speed angiography on the lesion 200. Executing Interactive Phi-Motion 300. Identifying the FV 400. Photocoagulating the FV 500. In a preferred embodiment of the invention, the method 100 is used to treat AMD related CNVs in humans.

25 0037 High-speed angiography 200 is performed using any suitable visualizing composition and obtaining high-speed images showing the visualizing composition filling the vessels in the region of interest. Preferably, a CNV and its associated feeder vessels are visualized using Indocyanine Green Dye Fluorescence Angiography. ICG dye is administered to the subject intravenously and allowed to perfuse through the subject's  
30 vasculature. Visualization is preferably effected by irradiating the area of interest with a laser light of a type and in an amount sufficient to cause the ICG dye to fluoresce.

0038 A preferred dosage of ICG, for visualizing FVs, is about 7.5 mg administered at a concentration of about 25mg/ml in a volume of approximately 0.3ml administered intravenously. Only one bolus is required per imaging sequence but multiple boluses may be employed. A concentration of about 0.025mg/ml in blood theoretically produces  
5 the most fluorescence from the fundus of a mammalian eye. Additionally, in some embodiments of the invention, administration of ICG intravenously is followed by a 5ml saline flush. The saline flush is used to rapidly push the bolus out of the cubital vein and into the vasculature within the thoracic cavity.

0039 Activation of the dye is preferably effected using a laser light source in the range  
10 of about 780nm-830nm. When visualizing a CNV and its associated feeder vessels in a mammalian eye, the laser light used to excite the dye preferably irradiates a target site of about 1cm<sup>2</sup> using about 20-100 mW of average power, although up to 230mW can be used. Irradiation of the target area with laser light is preferably effected for about 10-20 seconds.

0040 Capturing the sequence of high-speed images of the fluorescing vasculature can  
15 be accomplished by numerous means which are known and will be apparent to a person skilled in the art. Images are preferably captured as high-speed angiographic images on a CCD camera and stored in memory as one subject sequence. Using the preferred dosages above, high-speed images are typically recorded at a preferred rate of about 30  
20 frames/sec for 10-20secs in order to capture the fluorescence filling the vessel. According to this preferred embodiment of the invention, a typical subject sequence therefore is comprised of about 300 images.

0041 While the above represents the preferred parameters for capturing high-speed  
25 angiographic images of a CNV, it is well known in the art that other dosages, light parameters and capture speeds are also effective to produce fluorescence in the eye such that the CNV and its associated feeder vessels can be visualized and angiographically captured.

0042 Following the capture of high-speed angiographic images of the lesion and its  
30 associated FVs 200, Interactive Phi-Motion 300 is then performed on the sequence of high-speed images. Phi-motion is a phenomenon first identified by Wertheimer in 1912, it refers to the visual perception of motion where none exists, like a cinematic. By

utilizing phi-motion, in conjunction with dynamically manipulable parameters, IPM 300 allows for the subsequent improved identification and visualization of an FVs and most notably the direction of blood flow through the FV 400.

0043 Following identification of an FV suitable for treatment, photocoagulation of the vessel feeding the lesion is performed 500. Targeting of the photocoagulation treatment beam is based upon the information previously derived from visualization and identification of the lesion and its associated FVs 400 through IPM 300. Photocoagulation is effected by applying radiation of a kind and amount sufficient to effect an occlusion of the target vessel. It is believed that such occlusion occurs by increasing the temperature of the feeder vessel, resulting in either cauterization of the vessel or clotting of the blood within the vessel. As a result, the rate of blood flow through the vessel is reduced.

0044 In a preferred embodiment of the invention, DEP is performed by previously injecting the subject with a radiation absorbing dye such as ICG dye. Photocoagulation is thus enhanced by utilizing the radiation absorbing properties of the ICG dye to perform dye enhanced photocoagulation of the FV. Preferably, an approximately 810nm treatment laser is used at about 400-600mW for about 1.0-1.5 seconds. This produces about 0.4J-0.9J of energy sufficient to photocoagulate the vessel in the presence of ICG.

0045 The lesion is therefore attacked by cutting off the lesion's blood supply. This has the effect of starving the lesion and immediately reducing the hemodynamic pressure. Typical parameters for photocoagulation and DEP have been provided as preferred values and should not be construed as a limitation on the claims of the present invention

0046 Referring to figure 2, another broad aspect of the present invention provides a method for visualizing blood flow through blood vessels using IPM 300. IPM is comprised of the following steps. A subject sequence of previously captured high-speed angiographic images is retrieved 310. Limits defining a sequential subsequence, representing the period of interest, are received 320. Dynamic parameters are then received 330. Once a run instruction is received 340, the subsequence is displayed in phi-motion 350 until stopped 360. During this display 350, parameter changes 370 are dynamically updated 380 in response to changes, by a user, in said dynamic parameters.

0047 The subject sequence is typically retrieved from memory in response to a user selecting a specific sequence identifier. The subject sequence of previously captured high-speed angiographic images which is retrieved 310 for IPM should contain the period of interest. Therefore, the sequence should show the dye front entering and filling  
5 up the vessels in the lesion. Typically, a subject sequence is selected by a user and retrieved from a memory means.

0048 Limits representing a subsequence of the subject sequence is then received 320. Typically, these limits are selected by a user by defining a frame and a number of frames surrounding, following or preceding the defined frame, or preferably, by defining a first  
10 and last frame. The subsequence should define the period of interest, namely, the subsequence should contain that portion of the sequence that shows the visualizing dye entering the vessels, particularly the FV, associated with the lesion. The subsequence will be the only portion of the sequence undergoing IPM, thus, the longer the subsequence, the longer the IPM will take. Typically, using the preferred capture speeds  
15 and parameters above, about 30 frames are defined as the subsequence although any number of frames may be chosen depending on what the user wishes to visualize.

0049 Following the defining of the subsequence, the dynamic parameters are received 330. In a preferred embodiment of the invention, there are four dynamic parameters associated with IPM: speed, interval, direction and pixel brightness. The dynamic  
20 parameters can be updated in real time in response to user input at any time, including during the display in phi-motion.

0050 The speed parameter defines the speed at which the angiographic images are displayed in phi-motion. Typically, the speed parameter is quantified in frames per second, one frame representing one angiographic image in the subsequence.

25 0051 The interval parameter defines whether every image in the subsequence will be displayed. For example, in one embodiment of the invention, entering a value of two (2) will result in the display of every second image in the subsequence in phi-motion. The interval parameter may thus be adjusted to effect a display of every  $n^{\text{th}}$  image (i.e. second, third, fourth...etc.) during phi-motion display.

30 0052 The direction parameter defines the direction of the phi-motion display. In a preferred embodiment of the invention, the direction parameter can define running phi-

motion in a continuous forward loop, continuous backward loop or continuous bounce. Selecting continuous bounce would result in a continuous display, in phi-motion, of the subsequence of angiographic images from first image to last image, last to first, first to last...etc.

- 5    0053    The brightness parameter defines the relationship between collected intensity values and displayed intensity values. By manipulating the brightness parameter, pixels having a specific intensity on the collected angiographic image are adjusted to a different intensity on the phi-motion displayed angiographic image.

- 10    0054    Referring to figure 3, in a preferred embodiment of the invention, the brightness parameter is received and adjusted by manipulation of a Look-Up Table. The x-axis represents the collected intensity value and the y-axis represents the displayed intensity value. Typically, by default, the brightness parameter is set so that the collected and displayed intensity values are directly proportional and represented by a linear line with a slope of one. In this example, there are three control points in the LUT. There are two  
15    control points at the opposite corners and one control point in the middle. By displacing the control points, the user can manipulate the relationship between collected and displayed intensity values. Referring to figure 4, the control point in the middle of line has been moved upwards in response to user manipulation, typically by clicking and dragging a pointing device. The new line, still fixed at opposite corners is now  
20    comprised of 2 line segments and defines a new and adjusted relationship between the collected and displayed intensity values. Referring to figure 5, new points may also be added by a user, such as by clicking a pointing device on part of the LUT, in order to further segment the line and further manipulate the relationship between collected and displayed intensity values. It is important to note that in this embodiment of the  
25    invention, it is not possible to move successive points on the line behind another, that is, to make the line double back in such a way that one collected intensity value corresponds to more than one displayed intensity value.

- 0055    These parameters can be dynamically modified during phi-motion display in order to better visualize the blood flow through the region of interest. This allows for  
30    improved identification of a vessel feeding a lesion and visualization of direction of blood flow.

0056 It will be apparent to those skilled in the art that additional parameters when adjusted dynamically during phi-motion, can be used in order to better visualize and identify feeder vessels and the direction of blood flow through them.

0057 Upon receiving an instruction to start the display in phi-motion 340, the angiographic images are displayed in phi-motion 350. Display in phi-motion is effected by displaying the angiographic images of the defined subsequence in series and according to the dynamic parameters. In a preferred embodiment of the invention, the phi-motion is displayed in a display window on a monitor.

0058 Changes to any of the dynamic parameters are detected 370 and updated 380 in real-time such that the phi-motion continues running. Therefore, by performing IPM, one can view the successive angiographic images displayed in phi-motion while dynamically changing parameters such as speed, interval, direction and pixel brightness in real-time.

0059 Significantly, the present invention of IPM has several advantageous effects over and above conventional methods. First, by visualizing a dye filling up the vessels in a particular region in phi-motion, one can readily identify vessels in connection with the CNV and the direction of blood flow in them hence identifying the feeder (afferent) vessels as differentiated from the draining (efferent) vessels. Identification of FVs is essential to the success of photocoagulation as a treatment for lesions. Second, improved visualization and identification of FVs is accomplished by being able to manipulate the dynamic parameters in real-time while phi-motion display of the angiographic images continue to loop. Manipulation of these four parameters (speed, interval, direction and pixel brightness) dramatically improves the ability to visualize the dye entering the vessels in the region of interest and thus enhances FV identification. Finally, all the above is accomplished by obtaining one high-speed set of angiographic images. There is no need to take separate successive angiograms, possibly with multiple boluses, while trying to adjust the parameters between captures based on the previous angiogram set.

0060 In another embodiment of the invention, sequential subtraction of images in the defined subsequence is effected prior to running the phi-motion in order to reduce noise. Sequential subtraction may be performed with registration which determines the amount of shift and rotation between successive images, allowing successive images to be aligned and thus optimizing sequential subtraction. In order to further reduce noise, a

Fourier Filter can be effected on the subtracted images. Methods relating to sequential subtraction, registration and Fourier filtering, as is disclosed by U.S. Patent No. 5,394,199 (which is hereby incorporated by reference), are well known in the art.

0061 Referring to figure 6, there is shown an overall system overview diagram of a preferred embodiment of the invention incorporating the use of IPM 600. In this embodiment, a subject's head 605 containing the subject's eye 610 is shown. An apparatus operationally disposed to capture high-speed images 620 is comprised of a viewing monitor 621, a head mount 622, a CCD camera 623, a camera mount adaptor 624, a modified fundus camera 625, a camera positioning control 626 and a power and instrumentation cabinet 627. A computer system 650 comprises a CPU 651, memory 652, such as a hard disk and random access memory, an imaging processor 653, a PC monitor 654 and one or more input devices 655.

0062 In practice, the subject's eye 610 contains the lesion of interest, such as an AMD-related CNV. As such, the subject's eye is a candidate for treatment by photocoagulation of the FV of the CNV. The subject places his/her head 605 into the head mount 622 which can be adjusted to align the subject with the rest of the apparatus 620. The camera positioning control 626 is used to adjust the modified fundus camera 625 in order to align the fundus camera 625 with the area of interest containing the CNV. This alignment is visualized using the viewing monitor 621, which is mounted on the head mount 622 and displays the view through the fundus camera 625.

0063 Once the subject has been administered a visualizing dye such as ICG, the CCD camera 623, mounted via a camera mount adaptor 624, takes a series of high-speed angiographic images which are stored in memory 652 on computer system 650. The conversion of analog images to digital form, both generally and through the use of imaging board buffers (i.e. EPIX<sup>tm</sup>), are well known in the art. Each series of high-speed images are given a unique identifier such that it may be retrieved from memory 652. Each image in a series is also given a unique identifier such that it may be retrieved from memory 652.

0064 A series of high-speed images are retrieved from memory 652, pursuant to a request by a user through one or more input devices 655, and displayed on the PC monitor 654 using image processor 653. The computer system 650, contains an operating

system capable of performing run-time operations. A computer program is stored in memory 652 which, when executed by the CPU 651, is comprised of instructions corresponding to the method of IPM 200. The user defines a subsequence to undergo IPM via input devices 655. Dynamic parameters are defined using one or more input devices 655. In response to a start signal by the user through an input device 655, the CPU 651 displays the subsequence in phi-motion, pursuant to the dynamic parameters, on the PC monitor 654 using image processor 653. Dynamic parameters are updated by the CPU 651 during phi-motion.

0065 Referring to figure 7, a graphical user interface ("GUI") 700 of one embodiment of the invention is shown. The GUI 700 is displayed on the PC monitor 654. The GUI 700 comprises a display window 780, a corresponding slider bar 785, a LUT display 790, a stored sequence window 710, a phi-motion segment window 715, a treatment image window 740, a start phi-motion button and a store phi-motion subset button.

0066 The display window 780 displays images in the stored sequence. The display window 780 also displays the subsequence in phi-motion when the phi-motion display is running. The slider bar 785 is used select individual angiographic images in the stored sequence or subsequence to be displayed. The LUT display 790 is the interface used by the user to manipulate the relationship between collected and displayed intensity values for the phi-motion subsequence referred to with respect to figures 3-5. The default relationship between collected and displayed intensity values, namely a directly proportional relationship, can be restored by selecting a reset transfer function button 792. Control points may be added to the LUT by right clicking a mouse on an LUT line segment within the LUT display 790. Control points may be removed by selecting a remove control point button 793. Control points are automatically removed in the reverse order of their placement. Upon removal, addition or adjustment of each control point, the LUT is re-calculated with the modified points.

0067 The stored sequence window 710 numerically displays the first and last frame numbers in the stored sequence. The phi-motion window 715 comprises the following areas in which user may input limits and parameters. The phi-motion subsequence is defined by a first and last image and by inputting the corresponding frame numbers into first 720 and last 725 image boxes in the phi-motion segment window 715. The speed parameter is entered in a speed parameter box 730 in frames per second. The interval



parameter is entered in an interval parameter box 735. The direction parameter is defined by selecting an appropriate direction button, forward 751, reverse 752, or bounce 753.

0068 Phi-motion display can be initiated by selecting the start phi-motion button 760, and a phi-motion subsequence with accompanying parameters may be saved to memory  
5 652 by selecting the store phi-motion subset button 770.

0069 Treatment images may be manipulated by using the treatment image window 740. An individual treatment image may be marked with a marker by selecting a mark/select image button 741 and using the mouse to click on the treatment image displayed in the display window 780. The most recently added marker may be removed  
10 by selecting the remove last marker button 742. An individual treatment image may be stored in memory 652 by selecting a store treatment image button 743. Finally, a user may exit the program by selecting an exit button 800.

0070 Although the invention has been described with reference to certain specific embodiments, various modifications thereof will be apparent to those skilled in the art  
15 without departing from the spirit and scope of the invention as outlined in the claims appended hereto.

THE EMBODIMENTS OF THE INVENTION IN WHICH AN EXCLUSIVE  
PROPERTY OR PRIVILEGE IS CLAIMED ARE DEFINED AS FOLLOWS:

- 5 1. A method for visualizing fluid flow through vessels having a visualizing composition flowing therethrough, said method comprising the steps of:
  - (a) selecting from a sequence of angiographic images a subsequence of angiographic images;
  - (b) reading a plurality of dynamic parameters, said dynamic parameters for controlling display of said angiographic images;
  - 10 (c) serially displaying said subsequence repetitively in accordance with said dynamic parameters; and
  - (d) providing an interface for dynamic user update of said dynamic parameters while displaying said subsequence.
- 15 2. The method according to claim 1, wherein one of said dynamic parameters comprises a speed parameter, said speed parameter defining a speed at which said subsequence is serially displayed.
3. The method according to claim 1, wherein one of said dynamic parameters comprises an interval parameter, said interval parameter defining a number "n" corresponding to serially displaying said subsequence by serially displaying every n<sup>th</sup> angiographic image.
- 20 4. The method according to claim 1, wherein one of said dynamic parameters comprises a direction parameter, said direction parameter defining a direction in which said subsequence is serially displayed.
- 25 5. The method according to claim 1, wherein one of said dynamic parameters comprises a pixel brightness function, said pixel brightness function representing a relationship between an original pixel intensity value and a displayed pixel intensity value.
6. The method according to claim 5, wherein said pixel brightness function is represented by a Look-Up table capable of being manipulated by said user.
- 30 7. The method according to claim 1, wherein said visualizing composition comprises a fluorescing dye.
8. The method according to claim 1, wherein said visualizing composition comprises indocyanine green dye.
- 35 9. The method according to claim 1, wherein one of said vessels is a blood vessel feeding blood to a lesion.

10. The method according to claim 1, wherein one of said vessels is a blood vessel feeding blood to an age-related macular degeneration associated choroidal neovascularization.
- 5 11. A computer readable memory storing statements and instructions for use in the execution in a computer of the method of claim 1.
12. An apparatus for visualizing fluid flow through vessels by displaying multiple angiographic images of a visualizing composition flowing through said vessels, comprising:
- 10 (a) a means for selecting from a sequence of angiographic images a subsequence of angiographic images;
- (b) a means for reading a plurality of dynamic parameters, said dynamic parameters for controlling display of said angiographic images ;
- (c) a means for serially displaying said subsequence repetitively in accordance with said dynamic parameters; and
- 15 (d) a means for providing an interface for dynamic user update of said dynamic parameters while displaying said subsequence.
13. A computer program product, comprising: a memory having computer-readable code embodied therein for displaying the flow of a visualizing composition through blood vessels comprising:
- 20 (a) code means for selecting from a sequence of angiographic images a subsequence of angiographic images;
- (b) code means for reading a plurality of dynamic parameters, said dynamic parameters for controlling display of said angiographic images ;
- 25 (c) code means for serially displaying said subsequence repetitively in accordance with said dynamic parameters; and
- (d) code means for providing an interface for dynamic user update of said dynamic parameters while displaying said subsequence.
14. A method for treating a lesion of an animal, the animal having at least one blood vessel that carries blood to the lesion, comprising:
- 30 (a) administering a visualizing composition comprising a fluorescent dye;
- (b) capturing a plurality of angiographic images of a pre-selected area surrounding said lesion;
- (c) visualizing the flow of said visualizing composition through said lesion using the method of claim 1;
- 35 (d) identifying said blood vessel;

- (e) applying energy to said blood vessel, of a type and an amount sufficient to reduce the rate of blood flow through said blood vessel.
- 15. The method according to claim 14, wherein said fluorescent dye is indocyanine green dye.
- 5 16. The method according to claim 14, wherein said lesion is an age related macular degeneration associated choroidal neovascularization in a human.

Figure 1

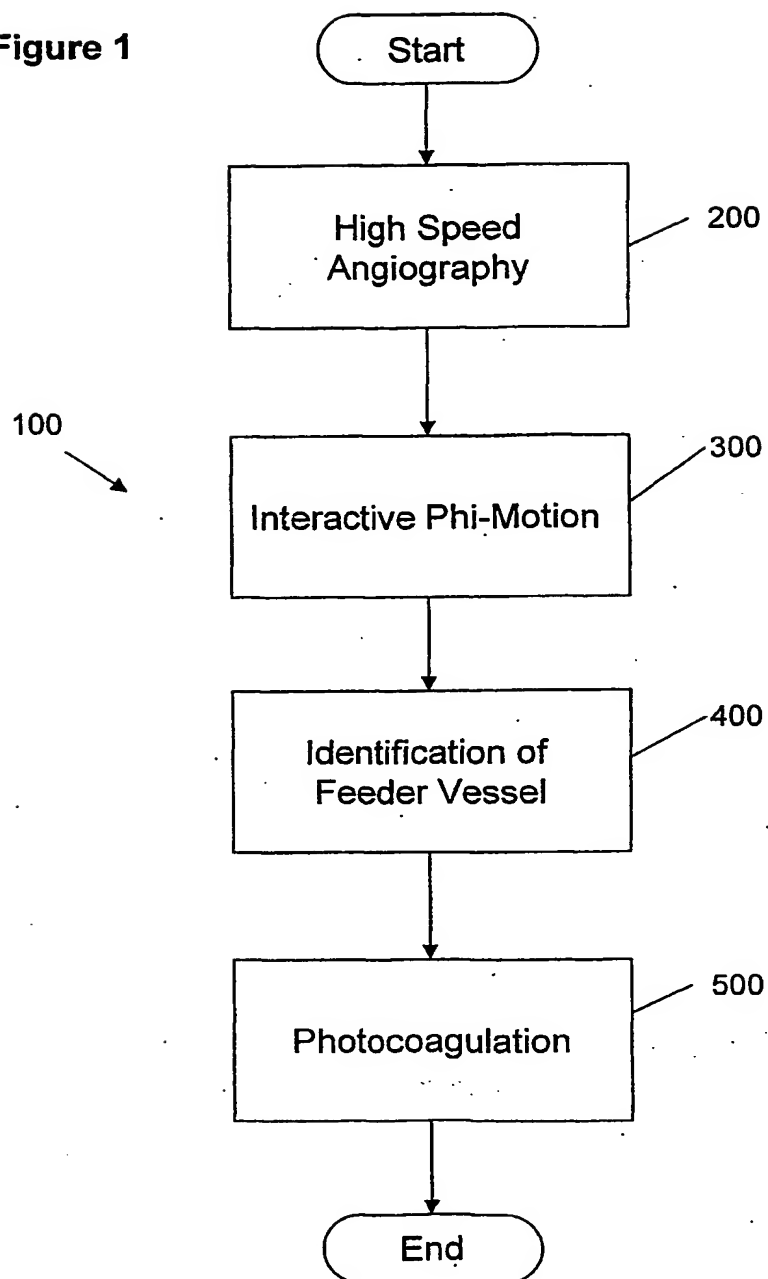
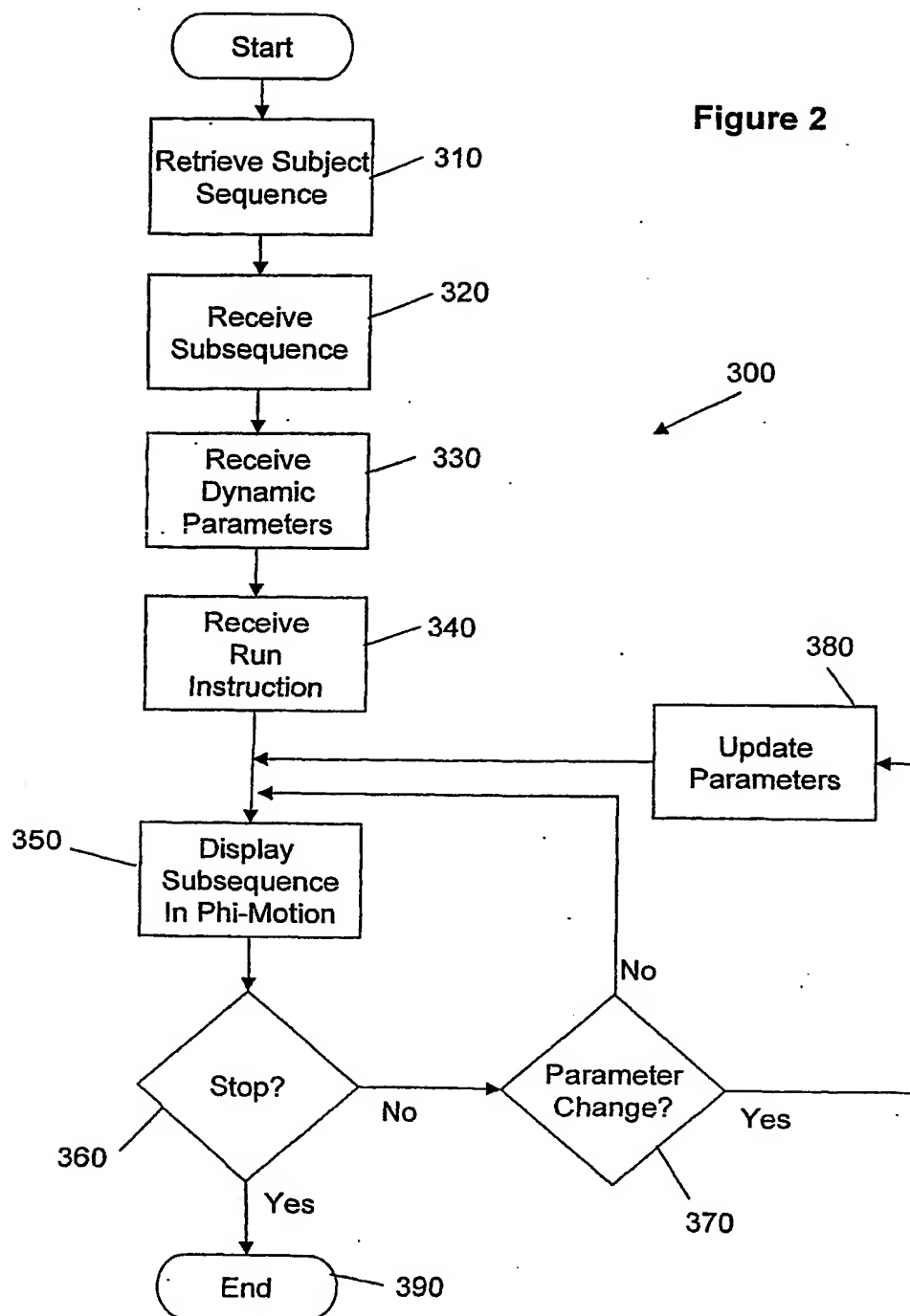


Figure 2



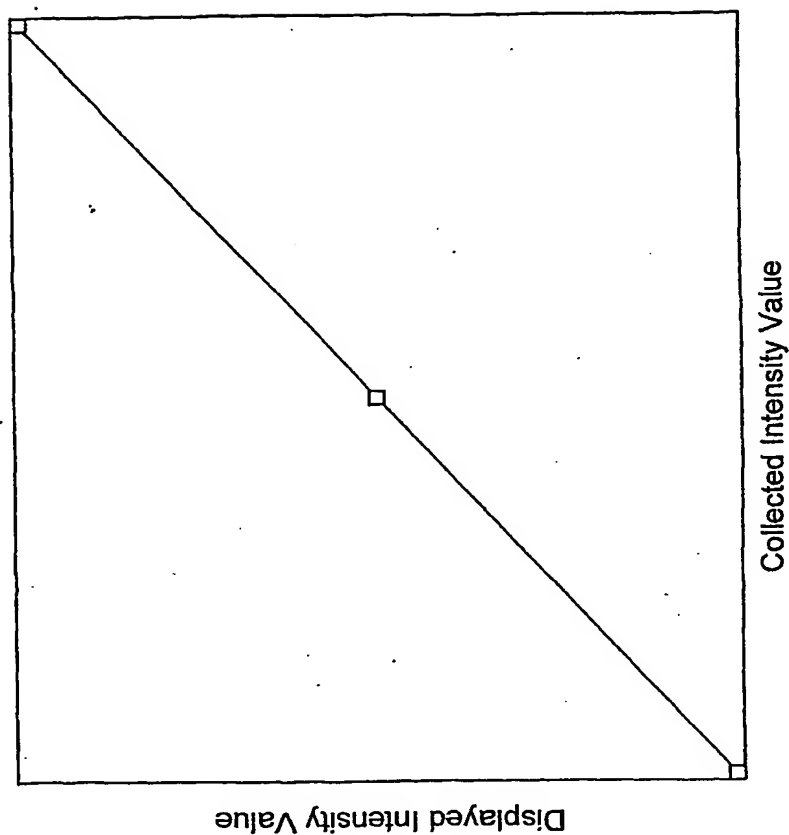


Figure 3

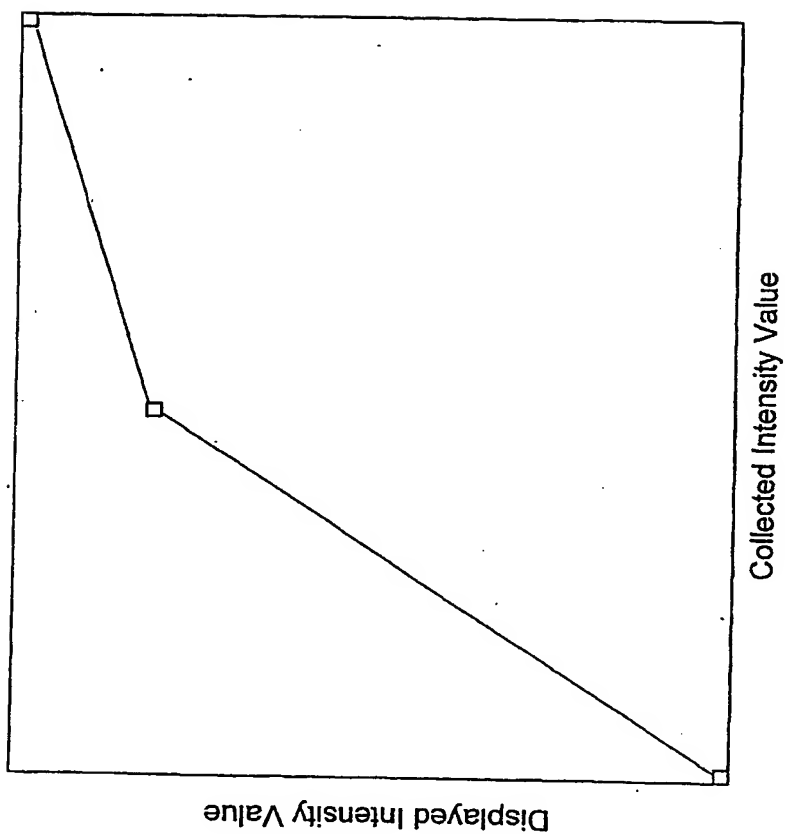


Figure 4



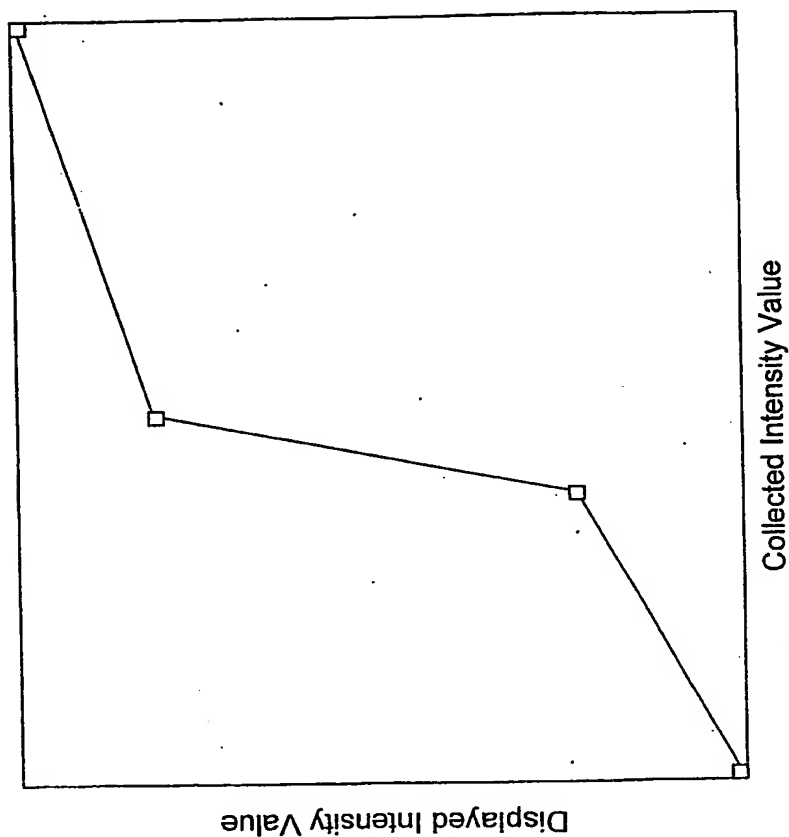


Figure 5

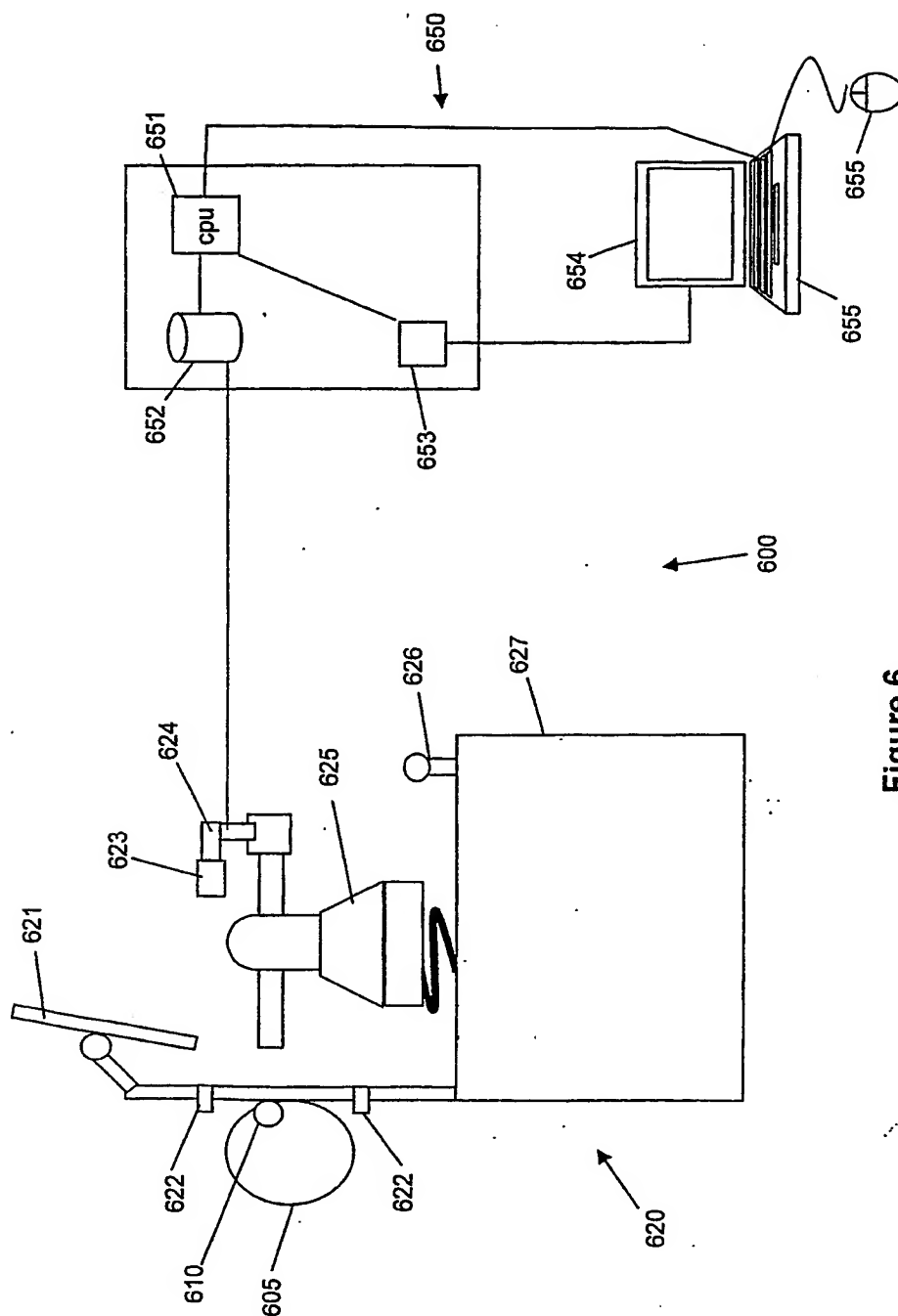
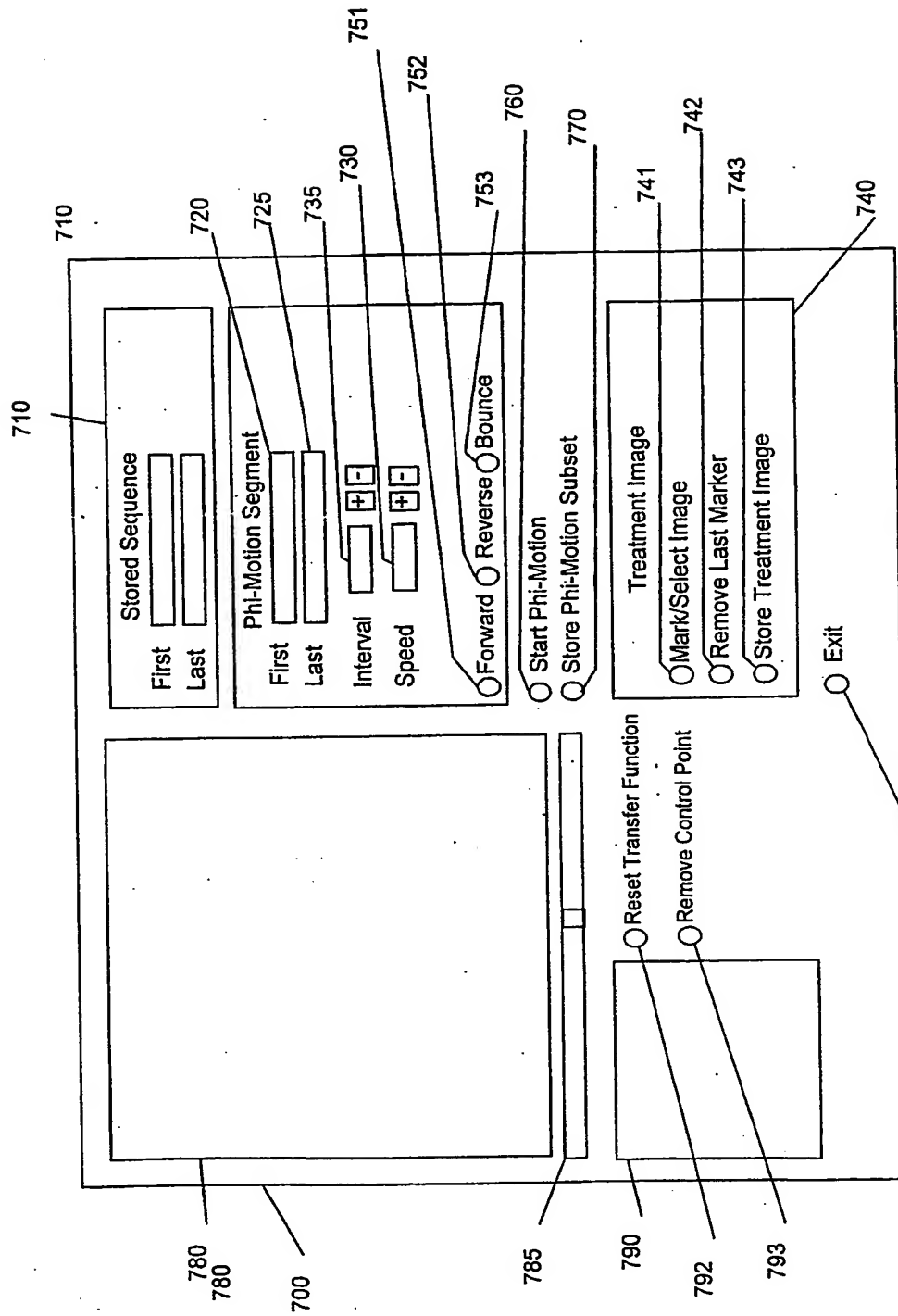


Figure 6



## INTERNATIONAL SEARCH REPORT

International Application No.

PCT/CA 03/00395

A. CLASSIFICATION OF SUBJECT MATTER  
IPC 7 A61B3/12

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
IPC 7 A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)  
EPO-Internal

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 6 350 238 B1 (TORP HANS ET AL) 26 February 2002 (2002-02-26) column 2, line 32 - line 57 column 10, line 24 - line 36	1,2, 11-13
Y	---	7-10
Y	US 5 394 199 A (FLOWER ROBERT W) 28 February 1995 (1995-02-28) cited in the application column 3, line 47 - column 5, line 3	7-10
A	---	1-6, 11-13
P, X	US 2002/035326 A1 (KAMIYAMA NAOHISA) 21 March 2002 (2002-03-21) paragraphs '0011!-'0018!, '0059!, '0066!, '0067! --- -/-	1,2, 11-13

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

## \* Special categories of cited documents :

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\*G\* document member of the same patent family

Date of the actual completion of the international search

28 July 2003

Date of mailing of the international search report

06/08/2003

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## INTERNATIONAL SEARCH REPORT

International Application No

PCT/CA 03/00395

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 6 158 864 A (NISHIHARA HIROSHI ET AL) 12 December 2000 (2000-12-12) column 2, line 43 -column 3, line 40 column 6, line 43 - line 67	1-13
A	WO 01 28405 A (TRUSTEES OF THE UNIVERSITY OF) 26 April 2001 (2001-04-26) page 1, line 18 -page 2, line 13 page 3, line 11 -page 5, line 2 page 8, line 4 -page 9, line 14	1-13

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/CA 03/00395

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 14-16  
because they relate to subject matter not required to be searched by this Authority, namely:  
Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

**INTERNATIONAL SEARCH REPORT**  
Information on patent family members

International Application No  
**PCT/CA 03/00395**

Patent document cited in search report		Publication date		Patent family member(s)	Publication date
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			WO	0128405 A2	26-04-2001
			US	6454410 B1	24-09-2002

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